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09/457,421	12/07/1999	ALAN A. DAVIS	AHP92038-2-C	7663

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/457,421	DAVIS ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claim 41 is added. Claims 26-41 are pending and under examination.

Claim Objections

2. Claim 36 is objected to because of the following informalities: Ranges are traditionally expressed in the following format, lower bound range then upper bound range. In the instant, claim 36 recites first an upper bound, $1x10^{10}$, then a lower bound, $8x10^{8}$. Such expression of ranges is not conventionally recognized. It is suggested that Applicant modifies the claim to reflect the conventionally recognized descriptor of ranges.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 36, 39 and 41 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 36 recites a booster dosage range of about $1x10^{10}$ to $8x10^{8}$ pfu of virus. The Examiner cannot find support for this limitation, nor has Applicant pointed the

specification for specific support of the instant range in Applicant's 09/04/03 preliminary amendment.

Additionally, support from the original disclosure for the following claims: 39 and 41.

Claim 39 is directed to the administration of a composition that comprises a deletion in the E3 gene and a deletion in the E1 gene. The specification only teaches of a deletion in the E3 gene region. Additionally, the specification also suggests that a deletion in the E1 region can also be used. However, nowhere in the specification is a deletion in both the E3 and E1 region is discussed. Furthermore, nowhere in the specification is a deletion to the E5 region is discussed. Support for the limitation recited in claim 37 cannot be found in the original disclosure nor did Applicant specifically point to the specification for support of the limitation that is recited in claim 39 in Applicant's 09/04/03 preliminary amendment.

Claim 41 is directed to the administration of a composition that comprises a recombinant adenovirus comprising the HIV-1 gp120 sequence, wherein the sequence is the MN strain gp120 sequence or the LAV strain gp120 sequence. Nowhere in the specification does Applicant teach of the composition that is recited under claim 41. Support for the limitation recited in claim 41 cannot be found in the original disclosure nor did Applicant specifically point to the specification for support of the limitation that is recited in claim 41 in Applicant's 09/04/03 preliminary amendment.

Applicant is required to cancel the new matter or point to the specification for specific support of the matter recited in claims 36, 39 and 41.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 26-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hung et al. (Nat. Immun. Cell Growth Regul., 1990; 9(3): 160-164.) in view of Davis et al., U.S. Patent No. 4920209.

The claims are directed at a method for producing an immune response against HIV-1 infection in a human comprising administering to the human an immunogenic composition comprising an intranasal or an intramuscular dosage of a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid encoding the HIV-1 gp160 or gp120 polypeptide sequence and a polyadenylation signal sequence. The claims further requires: i) that said method be followed by the step of administering one or more intranasal or intramuscular booster dosages of the recombinant adenovirus; which is further followed by one or more intramuscular injections of an HIV-1 antigen polypeptide dosage, wherein the polypeptide is a gag polypeptide an env polypeptide or a combination thereof; ii) the adenovirus is a serotype 4, 5 or 7 adenovirus; ii) the expression cassette further comprises the coding sequence for the HIV-1 rev gene inserted in the frame after the HIV-1 gp160 or gp120 sequence and before polyadenylation signal sequence; iii) the HIV-1 gp160 and gp120 sequence is of the MN or LAV strain; iv) the HIV-1 gp 160 sequence is replaced by a sequence

encoding the gag-pro region of HIV-1; v) the intranasal dosage is about $1x10^7$ pfu of virus; vi) the intranasal booster dosage is in the range of $1x10^7$ to $1x10^8$ pfu of virus; vii) the intramuscular booster dosage is in the range of $1x10^{10}$ to $8x10^8$ pfu of virus; viii) the antigen polypeptide dosage comprises between 200ug to .5mg of antigen polypeptide; ix) the adenovirus comprises a deletion in the E3 gene; x) the adenovirus comprises a deletion in the E3 gene and a deletion in the E1 gene or E5 gene; and xi) the adenovirus comprises a deletion in the E1 gene.

Hung et al. teaches an immunogenic composition comprising an intranasal or an intramuscular dosage of a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the HIV-1 envelope polypeptide sequence, which is gp160--which comprises gp120 and gp41, and a polyadenylation signal sequence. The adenovirus taught by Hung et al. of serotype 7 adenovirus. Hung et al. also teaches a composition comprising nucleic acid sequence encoding for the HIV-1 gag/pol regions instead of a nucleic acid sequence encoding the HIV-1 envelope polypeptide sequence. The composition of Hung et al. is in an intranasal and intramuscular form. Additionally, the composition of Hung et al. comprises a deletion in the E3 gene.

Hung et al. does not teach administering the composition to a human. However, Hung et al. suggested that the composition can be used as live recombinant vaccines. One of ordinary skill in the art at the time the invention was made would have been motivated to administer this vaccine to a human to induce an immune response against HIV-1 infection. One of ordinary skill in the art at the time the invention was made

would have had a reasonable expectation of success for doing so because Hung et al. teaches of vaccines comprising recombinant adenovirus that expresses HIV-1.

Additionally, it would have been obvious for one of ordinary skill in the art at the time the invention was made to experiment with various methodology of administrating the composition, such as in a prime and boost methodology. One of ordinary skill in the art at the time the invention was made would be motivated to practice said methodology with the composition of Hung et al. in a search for an administration methodology that would render the most beneficial immune response against HIV-1 infectivity. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because such experimentation is part of routine experimentation to arrive at an optimal administration methodology.

In addition, it would have been obvious for one of ordinary skill in the art at the time the invention was made to further administer to the subject, intramuscular injections, doses of an HIV-1 antigen polypeptide, wherein the polypeptide is gag, env, or combination thereof. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to further enhance the beneficial immune response that is observed in the patient against HIV-1 infectivity. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because such practice is part conventional experimental practice.

Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to experiment with the antigen dose amounts as part of routine experimentation. One of ordinary skill in the art at the time the invention was made

would have been motivated to so to determine the optimal dosage amount to administer in a subject to optimize the immune response in said subject against HIV infectivity. One of ordinary skill in the art would have had a reasonable expectation of success for doing so because such practice is part conventional experimental practice.

Hung et al. does not teach the insertion of a coding sequence for the HIV-rev gene in the frame after the HIV-1 gp160 sequence and before the polyadenylation signal sequence. However, Hung et al. teaches that expression of HIV-1 env. is enhanced in the presence of rev protein. One of ordinary skill in the art at the time the invention was made would have been motivated to take the teaching of Hung et al. and modify the composition of Hung et al. by adding a rev protein. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Hung et al. teaches how to express HIV-1 env in recombinant adenovirus.

As noted above, Hung et al. teaches of HIV-1; Hung et al. does not specify the strain of HIV-1, such as MN or LAV. However, it would have been obvious for one of ordinary skill in the art at the time the invention was made to take the teaching of Hung et al. and expand it to different types of HIV-1 strains. One of ordinary skill in the art at the time the invention was made would have been motivated to modify the composition of Hung et al. with envelope proteins from various strains of HIV-1 to provide a beneficial immune response that is specific to those that are infected with a specified strain of HIV-1. One of ordinary skill in the art at the time the invention was made would

have had a reasonable expectation of success for doing so because Hung et al. teaches how to make recombinant adenovirus that expresses HIV-1 envelope protein.

Hung et al. does not teach of a deletion in the E3 gene in conjunction with a deletion in the E1 gene. Additionally, Hung et al. does not teach a deletion in only the E1 gene. However, Davis et al. teaches that a deletion in the early region 1 or early region 3, E1 and E3, or both are expendably to maximize the length of the foreign nucleic acid sequence that can be inserted into the vector. It would have been obvious for one of ordinary skill in the art at the time the invention was made to combine the teaching of Hung et al. and Davis et al. One of ordinary skill in the art at the time the invention was made would have been motivated to introduce a deletion in the E3, E1, or both regions to accommodate the foreign nucleic acid sequence. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Davis et al. teaches that the E3 and E1 regions are expendable to maximize the length of the foreign nucleic acid sequence that can be inserted into the vector and Hung et al. teaches of adenovirus vectors that comprises a deletion in the E3 region.

Lastly, Hung et al. does not teach dose range of the virus that is instantly claimed. However, it would have been obvious for one of ordinary skill in the art at the time of the claimed invention to experiment with the dosage amount of the virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to arrive an optimal virus dosage amount for each specific group of subjects, such as infants, teenagers, and adults. One of ordinary skill in the art at the time the

invention was made would have had a reasonable expectation of success for doing so because such practices is part of conventional laboratory practice.

Therefore, for each instance, one of ordinary of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the claimed invention, absent unexpected results to the contrary.

7. Claims 26-31 and 33-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanda et al. (Int. Rev. Immunol., 1990; 7(1): 67-77. or Virology, 1990; 175: 535-547; in the alternative) in view of Davis et al., U.S. Patent No. 4920209.

Chanda et al. teaches an immunogenic composition comprising an intranasal or an intramuscular dosage of a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the HIV-1 envelope polypeptide sequence, which is gp160--which comprises gp120 and gp41, and a polyadenylation signal sequence. The adenovirus taught by Chanda et al. of serotype 7 adenovirus. The composition of Chanda et al. is in an oral vaccine form, thus it is in an intranasal and intramuscular form. Additionally, the composition of Hung et al. comprises a deletion in the E3 gene.

Chanda et al. does not teach administering the composition to a human. However, Chanda et al. suggested that the composition can be used as live recombinant vaccines against infectivity. One of ordinary skill in the art at the time the invention was made would have been motivated to administer this vaccine to a human to induce an immune response against HIV-1 infection. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success

for doing so because Chanda et al. teaches of vaccines comprising recombinant adenovirus that expresses HIV-1.

Additionally, it would have been obvious for one of ordinary skill in the art at the time the invention was made to experiment with various methodology of administrating the composition, such as in a prime and boost methodology. One of ordinary skill in the art at the time the invention was made would be motivated to practice said methodology with the composition of Chanda et al. in a search for an administration methodology that would render the most beneficial immune response against HIV-1 infectivity. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because such experimentation is part of routine experimentation to arrive at an optimal administration methodology.

In addition, it would have been obvious for one of ordinary skill in the art at the time the invention was made to further administer to the subject, intramuscular injections, doses of an HIV-1 antigen polypeptide, wherein the polypeptide is gag, env, or combination thereof. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to further enhance the beneficial immune response that is observed in the patient against HIV-1 infectivity. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because such practice is part conventional experimental practice.

Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to experiment with the antigen dose amounts as part of routine experimentation. One of ordinary skill in the art at the time the invention was made

would have been motivated to so to determine the optimal dosage amount to administer in a subject to optimize the immune response in said subject against HIV infectivity. One of ordinary skill in the art would have had a reasonable expectation of success for doing so because such practice is part conventional experimental practice.

Chanda et al. also teaches the insertion of a coding sequence for the HIV-rev gene with HIV-1 gp160 sequence in the recombinant adenovirus. However, Chanda et al. does not teach the insertion of a coding sequence for the HIV-rev gene in the frame after the HIV-1 gp160 sequence and before the polyadenylation signal sequence. One of ordinary skill in the art would have been motivated to experiment with the location of the rev protein in relation to the env protein because Chanda et al. teaches that expression of HIV-1 env is enhanced in the presence of rev protein. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Chanda et al. teaches how to express HIV-1 env in conjunction of HIV-1 rev proteins in recombinant adenovirus.

As noted above, Chanda et al. teaches of HIV-1; Chanda et al. does not specify the strain of HIV-1, such as MN or LAV. However, it would have been obvious for one of ordinary skill in the art at the time the invention was made to take the teaching of Chanda et al. and expand it to different types of HIV-1 strains. One of ordinary skill in the art at the time the invention was made would have been motivated to modify the composition of Chanda et al. with envelope proteins from various strains of HIV-1 to provide a beneficial immune response that is specific to those that are infected with a specified strain of HIV-1. One of ordinary skill in the art at the time the invention was

made would have had a reasonable expectation of success for doing so because Chanda et al. teaches how to make recombinant adenovirus that expresses HIV-1 envelope protein.

Chanda et al. does not teach of a deletion in the E3 gene in conjunction with a deletion in the E1 gene. Additionally, Chanda et al. does not teach a deletion in only the E1 gene. However, Davis et al. teaches that a deletion in the early region 1 or early region 3, E1 and E3, or both are expendably to maximize the length of the foreign nucleic acid sequence that can be inserted into the vector. It would have been obvious for one of ordinary skill in the art at the time the invention was made to combine the teaching of Chanda et al. and Davis et al. One of ordinary skill in the art at the time the invention was made would have been motivated to introduce a deletion in the E3, E1, or both regions to accommodate the foreign nucleic acid sequence. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because Davis et al. teaches that the E3 and E1 regions are expendable to maximize the length of the foreign nucleic acid sequence that can be inserted into the vector and Chanda et al. teaches of adenovirus vectors that comprises a deletion in the E3 region.

Lastly, Chanda et al. does not teach dose range of the virus that is instantly claimed. However, it would have been obvious for one of ordinary skill in the art at the time of the claimed invention to experiment with the dosage amount of the virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to arrive an optimal virus dosage amount for each specific group of subjects,

such as infants, teenagers, and adults. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because such practices is part of conventional laboratory practice.

Therefore, for each instance, one of ordinary of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the claimed invention, absent unexpected results to the contrary.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 40-41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,511,845. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to method of producing an immune response against HIV-1 infection in a human comprising recombinant adenovirus vectors that comprises HIV-1 envelope protein, which encompasses gp160, which comprises gp120.

10. Claims 26-41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/794876. Although the conflicting claims are not identical, they are not patentably distinct from each other because the immune response that is desired in the instant application encompasses protection of the primate against HIV-1 infection.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Emily Le
E.Le

James C. Housel 9/20/04

SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER